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NOVAK DRUCE DELUCA & QUIGG, LLP
1300 EYE STREET NW
SUITE 1000 WEST TOWER
WASHINGTON, DC 20005

EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/914,795	BERNDL ET AL.	
	Examiner	Art Unit	
	Sharmila Gollamudi Landau	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments and Remarks 10/2/07 is acknowledged. Claims **2-10 and 19** are pending in this application. Claims 1 and 11-18 stand cancelled.

Examiner's Remarks

The examiner suggests resolving issues such as purported lack of clarity of Office Actions, via a simple telephone conversation, rather than delaying prosecution of the application by filing non-responsive replies such as the response of April 20, 2007.

Further, it should be noted that the non-patent literature filed 7/16/07 will not be considered since the reference has not been properly filed in a Information Disclosure Statement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 2-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baert et al (6,365,188) in view of Stella et al (6,046,177).

Baert et al teach a solid mixture of cyclodextrin prepared via melt extrusion. The melt-extrusion mixture contains cyclodextrin and an active agent. See column 3, lines 26-40. Baert discloses that cyclodextrins increase the solubility of the insoluble drugs such as anti-fungals, specifically itraconazole. Any suitable compound may be utilized provided that the drug does not decompose at high temperatures. See column 2, lines 45-60. Baert teaches the use of substituted and unsubstituted cyclodextrins including beat-cyclodextrin, hydroxypropyl-β-cyclodextrin, and sulfobutylcyclodextrins. See column 7 in its entirety and specifically lines 61 and column 8, lines 4-10. Baert teaches melt-extrusion as the polymer extrusion technique wherein an active agent is embedded in one or more carriers. In this technique the active and excipients are molten in the extruder and hence embedded in the thermoplastic and thermomelting polymers. See column 3, lines 26-40. Additionally, the mixture may contain additives such as instant polyethylene glycol. See column 4, lines 34-42. The process includes a) mixing the cyclodextrin with the active agent and additives, b) mixing optional additives, c) heating the mixture until melting of one of the components occurs, d) forcing the mixture through one or more nozzles, and e) cooling the mixture to obtain a solid product. See column 4, lines 15-25. Although, a temperature of 239 degrees Celsius is exemplified, Baert discloses that different temperatures may be applied and discloses the method of ascertaining the required temperature. See column 5, lines 1-12. The extruder has counterotating screw with different shapes. See column 5. The melt-extruded mixture is preferably prepared without water or a solvent. The preferred ratio of the active to cyclodextrin is 1:3. See column 7, lines 64 to column 8, lines 4 and examples.

Baert et al do not specify the optional additives or the weight percent of the optional additives. Additionally, Baert does not teach the instant temperature of 170 degrees Celsius.

Stella et al teaches controlled release forms of solid formulations containing sulfoalkyl ether cyclodextrin (SAE-CD). The controlled release formulation contains a core containing an active agent, at least on SAE-CD, at least one rate controlling modifier, and at least one pharmaceutical acceptable excipient. See column 6, lines 1-7. The core may be made by several methods including melt extrusion. Note example 10. The release rate modifier provides either a delayed, sustained, timed, or targeted release of the active agent. See column 27, lines 40-50. Stella teaches varying the ratio of the rate controlling modifier and the drug such as 10:1 and 5:1, determines the release rate. The rate control modifier (exemplified HPMC) is varied from 25% to 50%. See column 17. Stella et al teach a controlled release device comprising 5% of prednisone; 35% SAE-β-CD; 50% HPMC (modified natural polymeric binder as defined by page 4 of the specification); and 10% lactose (excipient). See column 18, lines 27-35. Other release rate modifiers include HPMC, HPC, cellulose acetate butyrate, cellulose acetate propionate, cellulose propionate, carrageenan, cellulose acetate, cellulose nitrate, methylcellulose, hydroxyethyl cellulose, ethylcellulose, polyvinyl acetate, latex dispersions, acacia, tragacanth, guar gum, and gelatin. See column 38, lines 55-68.

Further, Stella teaches the use of binders such as celluloses, polyethylene glycols, polyvinylpyrrolidone, vinyl alcohol polymers, in order to obtain suitable products. See column 27, lines 5-30. Some of the binders named also function as the release rate modifier. See column 27, lines 48-50. The binder is utilized in different proportions in different examples. The example on column 37 utilizes 43% of EMDEX (a binder). Example 10 discloses a process utilizing melt extrusion wherein 2.5% of an active, 67.5% of SAE-CD, 10.5% PEG 6000, and excipients are melted at 60 degrees Celsius to form granules.

It would have been obvious at the time the invention was made to combine the teachings of Baert et al and Stella et al and utilize the a polymer as the additive in Baert's process. One would have been motivated to do so since Stella teaches the use of a rate controlling modifiers, such as exemplified HPMC, to control the release rate of the active to provide for a delayed, targeted, sustained, etc. dosage form. Therefore, it would have been prima facie obvious to add a polymer such as instant polymer in the instant amount, to modify the release rate of the dosage form. Further, it would have been obvious to utilize the polymer in the instant weight percent since Stella teaches the concentration of the rate controlling polymer determines the release rate. Therefore, depending on the release rate of the active, a skilled artisan would have been motivated to adjust the concentration accordingly. For instance, if one desired a slow release rate, a skilled artisan would have been motivated to add 50% of the polymer. A skilled artisan would have been motivated to do so with a reasonable expectation of success since Baert suggests the incorporation of optional additives including polymers.

With regard to the temperatures, the examiner points out that Baert teaches the use of various cyclodextrin derivates including sulfobutyl cyclodextrins, thus the melt extrusion temperature depends on the type of the cyclodextrin used and the components in the composition itself. Therefore, if one utilized a composition comprising the polymer additive and cyclodextrin, one would have used a temperature such as 60 degrees Celsius as taught by Stella et al. Further, a skilled artisan would have reasonably expected success in the variation of the temperature since Baert teaches that different temperatures may be applied and discloses the method of ascertaining the required temperature.

With regard to claims 9 and 10, absent the unexpectedness of mixing the polymer and cyclodextrin prior to mixing the drug, it is the examiner's position that the sequence in which the components are mixed and melted would not effect the process since all the components are rendered in a "plasticized", i.e. melted state.

With regard to the recitation, molecularly disperse the cyclodextrin and the active in the binder, the examiner points out that it is noted that applicant states that melt extrusion using the polymer in the instant concentration provides a solid solution wherein the active and cyclodextrin are molecularly dispersed in the polymer. Therefore, it is the examiner's position that the combination of references meet this limitation since Baert and Stella teach a melt extrusion and Stella teaches the instant concentration of the polymer.

Response to Arguments

Applicant argues that the examiner has used impermissible hindsight since Baert teaches away from using additives during the method of melt extruding the cyclodextrin and active. Applicant argues that Stella teaches "the term 'release modifiers' refers to a substance which will modify the rate of release of the therapeutic agent from the pharmaceutical formulation according to the instant invention". Applicant argues Stella provides no guidance as to which binders can be considered release rate modifiers.

Applicant's arguments filed 10/2/07 have been fully considered but they are not persuasive. It should noted that the instant rejection has been modified since applicant's amendments have broadened the scope to include alkyl celluloses and hydroxyalkyl celluloses. Therefore, the disclosure of Oshlack or Murata are not required since Stella teaches alkyl

celluloses and hydroxyalkyl celluloses. However, applicant's arguments pertaining to Baert and Stella will be discussed below since the examiner has retained these references.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In instant case, Baert teaches the use of any suitable additive during the process of melt extrusion process. Although Baert does not teach the instant additive, it is clear that any pharmaceutically acceptable additive may be used. Thus, the inclusion of an additive in the melt extrusion composition is not hindsight reasoning since this is clearly taught by Baert and Baert does not teach away from the adding additives such as rate controlling excipients in the melt extrusion process as argued by applicant. The secondary reference, Stella, teaches the use of release rate modifying polymers in a composition comprising cyclodextrin and an active agent. The purpose of the polymer is to manipulate the release rate wherein a higher concentration (50%) slows the release rate and a lower concentration provides faster release. Further, Stella teaches the dosage form may be made by melt extrusion wherein a temperature of 60 degrees Celsius is used. Thus, the melt extrusion temperature would vary according to the components in the composition. Although Baert exemplifies a temperature of 239 degrees Celsius, Baert discloses that different temperatures may be applied depending on the composition and discloses the method of ascertaining the required temperature. Clearly, the

temperature exemplified by Baert is not critical since as taught by Baert, it depends on the components in the composition. Thus, the manipulation of the temperature is not hindsight reasoning since the reference itself teaches the manipulation of the temperature as discussed above. Moreover, applicant argues that the temperature taught by Baert must melt either the cyclodextrin or the active agent. The examiner points out that the preferred drug, itraconazole, has a melting temperature of 166.2 degrees Celsius and as argued by applicant, Baert teaches a temperature must melt either the cyclodextrin or the active agent. Thus, clearly a temperature of less than 170 degrees Celsius would be suitable. Furthermore, the examiner points out that Baert teaches the use of various cyclodextrins including sulfoalkyl cyclodextrins. The examiner points out that depending on the type of cyclodextrin used, the melt extrusion temperature would also change. Thus, if one used a sulfoalkyl-cyclodextrin, then one would use the melt extrusion temperature taught by Stella et al, which is 60 degrees Celsius.

With regard to the claimed weight percents, the examiner points out that Stella teaches the use of rate controlling modifiers to control the release rate of the active to provide for a delayed, targeted, sustained, etc. dosage form. Thus if one desired a slow rate, a skilled artisan would have been motivated to add 50% of the rate-controlling polymer.

Regarding applicant's argument that Stella does not provide guidance on which binders can be considered release rate modifiers, the examiner directs applicant's attention to column 38, lines 58-66:

> It should be noted that in several of the above examples, binders such as EMDEX.TM. and polyox-0.4 M are replaceable by release controlling agents, or release rate modifiers, such as HPMC, HPC, cellulose acetate butyrate, cellulose acetate propionate, cellulose propionate, carrageenan, cellulose acetate, cellulose nitrate, methylcellulose, hydroxyethyl cellulose, ethylcellulose, polyvinyl acetate, latex dispersions, acacia, tragacanth, guar gum, gelatin, and the like.

Column 27, lines 43-51 also should be noted:

> The release rate modifier will assist in providing a controlled release of the therapeutic agent and can cooperate with other components in the formulation to provide either a delayed, sustained, timed, pH dependent, targeted, or further controlled delivery of the therapeutic agent. It will be understood that some of the binders mentioned herein can also be considered release rate modifiers.

Clearly, Stella teaches the function of a release rate modifier, i.e. to provide sustained, controlled, or timed release, and provides guidance on *what* polymers are considered release modifiers. Therefore, this "knowledge" has not been gleaned by applicant's disclosure.

The examiner further points out that the pharmaceutical art recognizes that polymers including cellulose derivatives function to modify the release rate of pharmaceutical compositions and that this property is not exclusive to a particular type of pharmaceutical. Meaning, the fact that Stella states that "the term 'release modifiers' refers to a substance which will modify the rate of release of the therapeutic agent from the pharmaceutical formulation according to the instant invention" does not mean that these polymers do not have the same function in different pharmaceutical formulations. The property of the polymer remains the same. This is evidenced by both Oshlack et al (6306438) and Murata et al (5,500,221). Both references teach Stella's polymers (HPMC, HPC, HEC, methylcellulose, etc) faction to modify the release rate of the pharmaceutical formulation.

Applicant cites KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007), wherein "the United States Supreme Court stated that the Graham v. Jolm Deere Co. of Kansas City, 383 U.S. 1 (1966), factors still control an obvious inquiry, and made clear that in order to establish a prima facie case of obvious 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' must be identified. Thus, in cases involving new chemical compounds, it remains necessary to identify

some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound."

The examiner points out that the KSR decision supports the examiner's prima facie obviousness rejection. Firstly, the examiner has adhered to the TSM test as explained clearly in the office action. It is noted that applicant does not address the examiner's motivation. Baert teaches additional additives may be incorporated during the process of making the melt extrusion composition comprising cyclodextrin and an active agent and Stella teaches a composition that comprises cyclodextrin, an active, and a release rate modifier, which may be prepared using melt extrusion. Stella clearly teaches the function of the release rate polymer and the weight percent. Therefore, a skilled artisan would have reasonably expected similar results and success from combining the references since 1) Baert suggests the use of optional additives including polymers during the melt extrusion process and 2) both Baert and Stella teach similar pharmaceutical composition comprising cyclodextrin and an active.

Secondly, as acknowledged by applicant, in the KSR decision, it was concluded that it was prima facie obvious to combine prior art elements according to known methods to yield a predictable result. In instant case, Baert teaches a melt extrusion process for making a composition comprising cyclodextrin, and active, and optional additives to prepare a pharmaceutical composition. Stella teaches a pharmaceutical composition comprising cyclodextrin and an active, which can be prepared using melt-extrusion. Stella further teaches the incorporation of a release rate polymer to provide for the desired release. Therefore, Stella teaches that the combination of elements, i.e. cyclodextrin, an active, and polymers such as cellulose derivatives, are known. The instantly claimed compounds are "not new" as argued by

applicant. Thus, to combine the elements of Baert's cyclodextrin and active with Stella's release rate polymer to yield a predictable results, i.e. a formulation with the desired release rate.

Applicant argues that Stella does not teach manipulating the concentration of the polymers and does not teach it is a result effective parameter.

The examiner disagrees. The examiner directs applicant's attention to column 17, lines 36-60:

> In the controlled release formulation according to the invention wherein the core is uncoated, **the ratio of release rate modifier to either one or both of the therapeutic agent or SAE-CD will have an impact upon the rate of delivery of the drug and the overall amount of drug delivered.** Accordingly, FIG. 18 depicts release profiles for various formulations wherein the amount of drug and cyclodextrin in the formulation have been kept constant and the amount of release rate modifier (HPMC) and diluent (lactose) have been varied. **Generally, as the ratio of release rate modifier to drug is increased, the release rate of the drug is decreased, and as the ratio of release rate modifier to cyclodextrin is increased, the release rate of the cyclodextrin is decreased.** In the specific example of FIG. 18, in this embodiment, when the ratio of release rate modifier to drug is approximately 10:1, approximately 40-50% of the drug will be released in about six hours after administration and approximately 55-60% of the drug will be released 12 hours after administration. When the ratio of release rate modifier to drug is approximately 5:1, the formulation will release approximately 65-75% of the drug after about six hours and approximately 75-90% of the drug 12 hours after administration. PD comprises 5% by weight of the formulation, SAE-CD comprises 35% by weight of the formulation, and increasing the amount of HPMC in the formulation is varied from 25% by weight to 50% by weight.

Cleary, Stella teaches the concentration of the release rate modifier is a result effective variable wherein the concentration determines the release rate.

Applicant argues that the references do not teach the amended limitation that the active and the cyclodextrin are molecularly dispersed in the polymeric binder to produce a solid solution. Applicant argues that in order to make this solid solution comprising this molecularly

dispersed cyclodextrin and active in the polymeric binder a high concentration of polymer must be utilized. Applicant argues that solid solutions are made by melt extrusion.

Firstly, the examiner points out that not only does the primary reference, Baert, teach a melt extrusion, but Stella also teaches the pharmaceutical may be made using melt extrusion. Therefore, the composition will necessarily be in a solid solution form wherein the cyclodextrin and active are molecularly dispersed. Secondly, the instant claims are directed to 50-98% of a polymer selected from a Markush group. The examiner points to column 18, lines 28-37, where Stella teaches a controlled release device comprising 5% of prednisone; 35% SAE-β-CD; 50% HPMC.

Therefore it is the examiner's position that the prior art renders the instant claims prima facie obvious for the reasons discussed above.

Claims 2-10 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuboi et al (6,063,393) by itself or in view of Klimesch et al (4,880,585).

Tsuboi teaches a method of controlling insects. The solid composition comprises a fungicide or insecticide and a substance that forms a matrix and functions as the solid carrier. This substance is preferably a polymeric carrier materials or mixture of polymeric materials. Tsuboi teaches the preference for polymers that can be processed as thermoplastics and have a processing time of 50-260 C. Tsuboi teaches various polymeric materials including vinyl polymers (see column 17, line 36), high molecular weight polyethylene glycols (PEG) (see examples 11 and 13), cellulose derivatives, etc. Example 3 discloses a process wherein 20 parts cyfluthrin, 0.1 parts triadminenol, 80 parts beta-cyclodextrin, 150 parts of a polymeric material Biopol polymeric carries, and 50 parts Carbowax 20M (polyethylene glycol polymeric carrier

MW about 17,500), are homogenized in an extruder at a temperature of 160°Celsius and then injection molded to a shaped form. The polymeric carrier is utilized in various weight percents including 50% and above. Note examples and example 3. With regard to claim 6, it is noted that the active and cyclodextrin implicitly form a complex during the process of melting the components and the reference does not explicitly state that the active and cyclodextrin are maintained in an uncomplexed state. Tsuboi teaches the type of shaping can be produced by any known method in the art. see column 23, lines 20-25.

Although Tsuboi suggests the use of vinyl polymers and uses high molecular weight polyethylene glycols (3000-7000MW and 7800-9000), one cannot immediately envisage the use of polyethylene glycols in example 3 specifically. Further, although Tsuboi suggests the use of vinyl alcohols, Tsuboi does not specify the use of polyvinylpyrolidone.

Klimesch et al teaches a method of continuous tableting using a molding calendar with opposite rollers (col. 1, lines 16-27). Klimesch teaches extrudable mixtures are mixtures of one or more active compounds with one or more auxiliaries, which are conventionally used in the preparation of pharmaceutical tablets and are pasty and therefore extrudable due to the melting or softening of one or more components. This process is known as melt-extrusion. These include polyvinylpyrrolidone (PVP), copolymers of N-vinylpyrrolidone (NVP) and vinyl acetate, copolymers of vinyl acetate and crotonic acid, partially hydrolyzed polyvinyl acetate, polyvinyl alcohol, ethylene/vinyl acetate copolymers, polyhydroxyethyl methacrylate, copolymers of methyl methacrylate and acrylic acid, cellulose esters, cellulose ethers, polyethylene glycol and polyethylene. Klimesch teaches the polymeric binder must soften or melt at from 50 to 180 degrees C. preferably from 60 to 130 degrees C. and the NVP polymers have a melt temperature

below 120 degree C. see column 3, lines 1-65. Klimesch teaches the process provides a simple, continuous method of tableting wherein the mixture is extruded and the still deformable extrudate is pressed between two rollers which are driven in opposite directions and possess depressions opposite one another in the roller shell (molding calendar), the form of these depressions determining the tablet shape. Thus, the process eliminates premixing (col. 1, lines 16-27 and 28-34).

Firstly, it would have been obvious to look at the guidance provided by Tsuboi and substitute the exemplified polymeric carriers with any of the suggested polymeric carriers including polyvinyl polymers, polyethylene glycols, and cellulose derivatives. One would have been motivated to do so with a reasonable expectation of success since Tsuboi suggests various polymers may be utilized including the instantly claimed polymers. Further, Tsuboi teaches the carrier can be one polymer or a combination of materials. For instance, example 3 teaches a mixture of polymeric materials as the carriers, i.e. Biopol and Carbowax 20M (PEG with a molecular weight of 17,500). However, it would have been obvious for a skilled artisan to formulate the dosage form wherein the polymeric matrix was made of one polymer such as Carbowax 20M. This is an obvious modification absent evidence of unobviousness.

Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Tsuboi and Klimesch and substitute the polymeric carrier taught in Tsuboi's example 3 and utilize the instantly claimed polymers. One would have been motivated to do so with a reasonable expectation of success since Tsuboi suggests the use of various polymers including vinyl polymers and high molecular weight polyethylene glycol polymers and Klimesch teaches polyvinylpyrolidone (a vinyl polymer) or

polyethylene glycol are known thermoplastic polymers used in melt extrusion processes. Therefore, to substitute melt extrusion polymer with another known and conventionally utilized melt extrusion polymer is prima facie obvious. It is noted that Tsuboi is directed to a plant treatment compositions and Klimesch is directed to pharmaceutical compositions; however the examiner points out that " it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention." In instant case, Klimesch is reasonably pertinent to the particular problem, i.e. the use of polymeric carriers in melt extrusion processes.

Regarding claims 3-4, it would have been obvious to a skilled artisan to utilize a molding calendar in the extrusion process since Tsuboi teaches the use of any known method to shape the product and Klimesch et al teach using mold calendaring to produce certain shapes.

Regarding claim 7, it is the examiner's position that EP would have similar, if not the same, functional properties since the prior art composition is substantially similar. See MPEP2112 IV, V and 2112.01.

Regarding claims 9 and 10, absent the unexpectedness of mixing the polymer and cyclodextrin prior to mixing the drug, it is the examiner's position that the sequence in which the components are mixed and melted would not effect the process since all the components are rendered in a "plasticized", i.e. melted state.

Regarding the recitation, molecularly disperse the cyclodextrin and the active in the binder, the examiner points out that it is noted that applicant states that melt extrusion using the polymer in the instant concentration provides a solid solution wherein the active and

cyclodextrin are molecularly dispersed in the polymer. Therefore, it is the examiner's position that the combination of references meet this limitation since the references teach melt extrusion using instant polymers in the instant amount.

Response to Arguments

Applicant argues that Tsuboi is directed to treatment of plants and Klimesch is directed to pharmaceutical tablets. Applicant argues that Tsuboi does not teach the polymers required in the amended claims. Applicant argues that there must be some reason for a skilled artisan to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.

Applicant's arguments filed 10/2/07 have been fully considered but they are not persuasive. Firstly, the examiner points out that Tsuboi renders the instant invention obvious over itself and it is noted that applicant has not addressed. Secondly, with regard to the combination of Tsuboi and Klimesch, the examiner directs applicant's attention to the two-prong test for non-analogous art, which is delineated in MPEP 2141.01. The test is that the reference must either be in the field of Applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned. As clearly set forth in the above rejection, although it is acknowledged that Tsuboi and Klimesch are not in the same field of endeavor and therefore fails the first part of the test; Klimesch meets the second prong of the test. In instant case, both Tsuboi and Klimesch are directed to making solid dosage forms using melt extrusion wherein an active and a polymeric carrier are melt-extruded. The only difference between the references is the active agent utilized. It is further noted that both references teach the same polymeric materials. The examiner points out that the intended use of the solid dosage

form, i.e. the incorporation of a plant-treating drug versus a pharmaceutical does not change the process of melt extrusion itself. Meaning, regardless of the specific active used, the process of melting the active agent and the polymer, i.e. melt extrusion, remains the same. Therefore, Klimesch is reasonably pertinent to the particular problem taught in Tsuboi, i.e. the use of polymeric carriers in melt extrusion processes.

Regarding, applicant's argument that the examiner is required to file an examiner's affidavit, it is unclear why applicant has cited this MPEP section, which is irrelevant to the above discussion. Obviously applicant's representative has misinterpreted MPEP 1.104(c)(D)(2). This section refers to "official notice" *without supporting evidence,* i.e. "[w]hen a rejection in an application is based on facts within the personal knowledge of an employee of the Office. In instant case, all the limitations are discussed and supported with references. Klimesch is the supporting document. The examiner has not made assertions such as "it is well known" or it is "common knowledge". Therefore, an examiner's affidavit is not required. The examiner suggests applicant's representative read MPEP 1.104(c)(D)(2) and MPEP 2144.02.

Therefore it is the examiner's position that the prior art renders the instant claims prima facie obvious for the reasons discussed above.

Conclusion

All the claims are rejected at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila Gollamudi Landau whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila Gollamudi Landau
Primary Examiner
Art Unit 1616